

AMENDMENTS TO THE CLAIMS

Claims 1-96 (Canceled)

97. (New) A transgenic mouse comprising a disruption in an endogenous ROR γ gene, wherein where the disruption is homozygous, the transgenic mouse lacks production of functional ROR γ protein and exhibits, relative to a wild-type mouse, a phenotypic abnormality selected from the group consisting of a spleen abnormality, a kidney abnormality, a liver abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones.

98. (New) The transgenic mouse of claim 97, wherein the spleen abnormality is increased weight of the spleen relative to a wild-type mouse.

99. (New) The transgenic mouse of claim 97, wherein the spleen abnormality is increased size of the spleen relative to a wild-type mouse.

100. (New) The transgenic mouse of claim 97, wherein the spleen abnormality is an increased spleen to body weight ratio relative to a wild-type mouse.

101. (New) The transgenic mouse of claim 97, wherein the kidney abnormality is increased weight of the kidney relative to a wild-type mouse.

102. (New) The transgenic mouse of claim 97, wherein the kidney abnormality is increased size of the kidney relative to a wild-type mouse.

103. (New) The transgenic mouse of claim 97, wherein the kidney abnormality is an increased kidney to body weight ratio relative to a wild-type mouse.

104. (New) The transgenic mouse of claim 97, wherein the kidney abnormality is elevated blood urea nitrogen, relative to a wild-type mouse.

105. (New) The transgenic mouse of claim 97, wherein the liver abnormality is increased weight of the liver relative to a wild-type mouse.

106. (New) The transgenic mouse of claim 97, wherein the liver abnormality is increased size of the liver relative to a wild-type mouse.

107. (New) The transgenic mouse of claim 97, wherein liver abnormality is an increased liver to body weight ratio relative to a wild-type mouse.

108. (New) The transgenic mouse of claim 97, wherein liver abnormality is elevated serum alanine aminotransferase.
109. (New) The transgenic mouse of claim 97, wherein the thymus abnormality is increased weight of the thymus relative to a wild-type mouse.
110. (New) The transgenic mouse of claim 97, wherein the thymus abnormality is increased size of the thymus relative to a wild-type mouse.
111. (New) The transgenic mouse of claim 97, wherein the thymus abnormality is an increased thymus to body weight ratio relative to a wild-type mouse.
112. (New) The transgenic mouse of claim 97, wherein the abnormality of the thymus is thymic cortical expansion and medullary reduction relative to a wild-type mouse.
113. (New) The transgenic mouse of claim 97, wherein the abnormality of the lymph nodes is depletion of lymph nodes relative to a wild-type mouse.
114. (New) The transgenic mouse of claim 97, wherein the abnormality of the lymph nodes is absence of lymph nodes.
115. (New) The transgenic mouse of claim 97, wherein the abnormality of the lymph nodes is depletion of gut associated lymphoid tissue ratio relative to a wild-type mouse.
116. (New) The transgenic mouse of claim 97, wherein the abnormality in the lymphocytes comprises lymphoid infiltrates.
117. (New) The transgenic mouse of claim 97, wherein the abnormality in the lymphocytes is consistent with lymphoma.
118. (New) The transgenic mouse of claim 117, wherein the transgenic mouse further comprises at least one of the following symptoms of disease: poor grooming, hypoactivity, increased thoracic girth, and increased abdominal girth, hepatosplenomegaly, enlarged thymus, ascites, weakness, squinting, hunching, cachexis, lethargy, and impaired respiration.
119. (New) The transgenic mouse of claim 97, wherein the bone marrow is pale.
120. (New) The transgenic mouse of claim 97, wherein the abnormality of the bones is brittleness.
121. (New) The transgenic mouse of claim 97, wherein the abnormality of the bones is attached white masses.
122. (New) A cell or tissue obtained from the transgenic mouse of claim 97.

123. (New) A method of producing a transgenic mouse comprising a disruption in an endogenous ROR γ gene, the method comprising:

- (a) introducing a targeting construct capable of disrupting the endogenous ROR γ gene into a murine embryonic stem cell;
- (b) introducing the murine embryonic stem cell into a blastocyst;
- (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein the pseudopregnant mouse gives birth to a chimeric mouse; and
- (d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in the endogenous ROR γ gene,

wherein where the disruption is homozygous, the transgenic mouse lacks production of functional ROR γ protein and exhibits, relative to a wild-type mouse, a phenotypic abnormality selected from the group consisting of a spleen abnormality, a kidney abnormality, a liver abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones.

124. (New) The transgenic mouse produced by the method of claim 123.

125. (New) A targeting construct comprising:

- (a) a first polynucleotide sequence homologous to at least a first portion of an endogenous ROR γ gene;
- (b) a second polynucleotide sequence homologous to at least a second portion of the endogenous ROR γ gene; and
- (c) a selectable marker gene located between the first and second polynucleotide sequences; wherein the targeting construct, when introduced into a murine embryonic stem cell, results in a transgenic mouse whose genome comprises a disruption in the endogenous ROR γ gene, wherein the transgenic mouse lacks production of functional ROR γ protein and exhibits, relative to a wild-type mouse, a phenotypic abnormality selected from the group consisting of a spleen abnormality, a kidney abnormality, a liver abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones.

126. (New) A murine embryonic stem cell comprising a disruption in an endogenous ROR γ gene, the disruption produced using the targeting construct of claim 125.

127. (New) A method of identifying an agent capable of modulating a phenotype associated with a disruption in an endogenous ROR γ gene, the method comprising:

- (a) administering a putative agent to a transgenic mouse whose genome comprises a homozygous disruption in the endogenous ROR γ gene, wherein the transgenic mouse lacks production of functional ROR γ protein and exhibits, relative to a wild-type mouse, a phenotypic abnormality selected from the group consisting of a spleen abnormality, a kidney abnormality, a liver abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones; and
- (b) determining whether the phenotype exhibited by the transgenic mouse in step (a) is modulated.